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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/047,710	01/15/2002	Ananda M. Chakrabarty	11170/3	3837

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EXAMINER	
YU, MISOOK	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/047,710	CHAKRABARTY ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-24 and 26-49* is/are pending in the application.

4a) Of the above claim(s) *17-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,24 and 26-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/1/02, 1/23/04*, 10/25/04, 03/02/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group IV, claims 40-48. As requested, group III invention is rejoined with the elected invention.

Claims 17-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 01/25/2005. Claims 17-24, and 26-49 (See Rule 1.126 below) are pending. Claims 23, 24, and 26-49 are examined on merits. The species election is withdrawn and search is expanded to other species.

Claim Objections

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 45-48 have been renumbered as claims 46-49, respectively.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23, 24, 33, 34-37, 39-41, and 43-46, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description rejection is made because the claims are interpreted as drawn to method of using a genus of products recited as "a cytotoxic factor, and a variant or derivative of the cytotoxic factor", "a variant or derivative thereof".

The applicable standard for the written description requirement can be found: MPEP 2163; University of California v. Eli Lilly, 43 USPQ2d 1398 at 1407; PTO Written Description Guidelines; Enzo Biochem Inc. v. Gen-Prove Inc., 63 USPQ2d 1609; Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111; and University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC 2004).

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

In this case, the only factor present in the claims is function of the product being claimed. There is not even identification of any particular portion of the structure that must be conserved in order to be "cytotoxic factor, a variant or derivative thereof".

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. A definition by function alone "does not suffice, to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Eli Lily*, 119 F.3 at 1568, 43 USPQ2d at 1406.

The specification discloses:

[0022] For the purposes of the description herein, the term "cytotoxic factor" refers to a factor secreted by a pathogenic microorganism and which stimulates cell death by necrosis or apoptosis. The term "ATP-dependent", when used to modify the term "cytotoxic factor" refers to a cytotoxic factor which acts to cause cell death in the presence of adenosine 5'-triphosphate (ATP). The term "ATP-independent", when used to modify the term "cytotoxic factor" refers to a cytotoxic factor which acts to cause cell death in the absence of ATP.

[0026] As used herein, the term "a variant or derivative thereof" refers to a compound or substance obtained by chemical modification or manipulation of genes encoding the compound or substance. When referring to a variant or derivative of a cytotoxic factor, the variant or derivative can be obtained by chemical modification of the cytotoxic factor, or by manipulation of genes encoding such cytotoxic factors, for example by altering the basic composition or characteristics of the cytotoxic factor, but not its toxicity. Similarly, a derivative of an inhibitor of a cytotoxic factor can include chemical modifications to the chemical structure of the inhibitor or manipulation of genes encoding the inhibitor. For example, the antibiotic penicillin can be chemically modified to provide derivatives that are more potent or have a wider spectrum than penicillin itself.

Based on the definition, in order to make "variant and derivative thereof" of a cytotoxic factor, one has to screen which other factor other than the art-known sequence of azurin, and cytochrome C551 is secreted by a by a pathogenic microorganism and which stimulates cell death by necrosis or apoptosis, followed by cloning of the DNA sequence encoding the factor. Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those

skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of cytotoxic factor, variant or derivative thereof, given that the specification has only described azurin, and cytochrome C551, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 23, 24, 33-36, and 39, 40, 41, 43, 45, and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by US PAT 5,681,810 (28 October 1997, the '810 patent from now on).

Claims 23, 24, 33-36, and 39, 40, 41, 43, 45, and 46 are interpreted as drawn to method of modulating melanoma (elected species) cell death either by administering to a patient a pharmaceutical comprising a cytotoxic factor, variant or derivative thereof, or

contacting melanoma cells with a cytotoxic factor, and a variant or a derivative of the cytotoxic factor, wherein the cytotoxic factor is a redox protein (claim 24).

The '810 patent teaches method of modulating melanoma (elected species) cell death either by administering to a patient a pharmaceutical comprising a cytotoxic factor, variant or derivative thereof, or contacting melanoma cells with a cytotoxic factor, and a variant or a derivative of the cytotoxic factor. Note columns 7, 8 10, 11 especially Example 6 at column 15, and claims 11-15.

Based on the definition of "necrosis" as "to make dead" according to Merriam-Webster Online dictionary downloaded from URL>>www.m-w.com on 4/25/2005, and the disclosure of the specification at Paragraph [0022] that defines cytotoxic factor to be a factor secreted by a pathogenic microorganism and which stimulates cell death by necrosis or apoptosis, and also at Paragraph [0026] that define "a variant or derivative thereof" to be a compound or substance obtained by chemical modification or manipulation of genes encoding the compound or substance, the diphtheria toxin or the variant or derivative thereof as graphically shown in Fig. 1 of the '810 patent meets limitation "a cytotoxic factor, variant or derivative thereof" because diphtheria toxin is from a factor secreted by a pathogenic microorganism and which stimulates cell death by necrosis or apoptosis. As for the diphtheria toxin being "a factor secreted by a pathogenic factor and which stimulates cell death by necrosis or apoptosis" as defined Paragraph [0022] of the instant specification, and a redox protein as recited in the instant claim 24, Voet et al., (Biochemistry, 1990, John Wiley & Sons, pages 415-417,

932, and 933 only) teach that diphtheria toxin is inherently a redox protein, and secreted by a by a pathogenic microorganism and which stimulates cell death.

Claims 23, 33, 34, 37, and 39, 40, 41, 43, and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by US PAT 5,972,899 (26 October 1999, the '899 patent from now on).

Claims 23, 24, 33, 34, 37, and 39, 40, 41, 43, and 44 are interpreted as drawn to method of modulating cancer cell death either by administering to a patient a pharmaceutical comprising a cytotoxic factor, variant or derivative thereof, or contacting cells with a cytotoxic factor, and a variant or a derivative of the cytotoxic factor, wherein the cytotoxic factor is a redox protein (claim 24), or induces apoptosis (claims 37, 44)

The 'the '899 patent teaches the claimed invention in the patent is method of cancer cell death either by administering to a patient a pharmaceutical comprising Shigella Ipa B toxin, which induces apoptosis. Note abstract, columns 3, 4, 7, 8, 38.

Claims 40, and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Zaborina et al., (1999, Infection and Immunity, vol. 67, pages 5231-42, A1 of IDS filed on 4/1/2002).

Claims 40, and 43 are interpreted as drawn to method of contacting cells with a cytotoxic factor, wherein the cytotoxic factor inhibits growth of the cells by killing the cells.

Zaborina et al., at page 5237-5239 under the heading "Physiolgical significance of the secretion of ATP-utilizing enzyme by mucoid *P. aeruginosa*" teach that secretion of the ATP-utilizing enzymes by mucoid *P. aeruginosa* inhibits or kills the cells being contacted by the secreted by the pathogenic microorganism. The ATP-utilizing enzymes secreted by mucoid *P. aeruginosa* of Zaborina et al., meets the limitation "a cytotoxic factor" in claim 40 because the specification at Paragraph [0022] defines as "the term "cytotoxic factor" refers to a factor secreted by a pathogenic microorganism and which stimulates cell death by necrosis or apoptosis."

Claims 40, and 42-44, 47-49 are rejected under 35 U.S.C. **102(a)** as being anticipated by Zaborina et al., (2000, Microbiology, vol. 146, pages 2521-30, A4 of IDS filed on 4/1/2002).

Claims 40, and 42-44, 47-49 are interpreted as drawn to method comprising contacting cells with a compound comprising azruin or cytochrome C551, wherein said compound inhibits growth of the cells by apoptosis, or by killing the cells.

Zaborina et al., teach method comprising contacting cells with a compound comprising azruin or cytochrome C551, wherein said compound inhibits growth of the cells by apoptosis, or by killing the cells. Note especially the abstract.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 23, 24, 26-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zaborina et al., (2000, Microbiology, vol. 146, pages 2521-30, A4 of IDS filed on 4/1/2002) in view of the '899 patent (cited above).

Claims 23, 24, 26-32 are interpreted as drawn to method of cancer treatment using a compound comprising azruin or cytochrome C551.

Zaborina et al., (2000) teach azruin or cytochrome C551 from pseudonmonas aeruginosa induce apoptosis.

Zaborina et al., do not teach administering to a cancer patient.

However, the '899 patent teach that cancer cells have a decreased ability to under apoptosis and bacterial proteins inducing apoptosis is useful in treating cancer. See abstract, and columns 7, and 8.

Therefore, it would have been obvious to one of ordinary skill in the art to use the claimed invention with a reasonable expectation of success because Zaborina et al., (2000) teach how to make the compound comprising azurn or cytochrome C551, and the '899 patent teach that bacterial proteins inducing apoptosis is useful in treating

cancer. One of skill in the art would be motivated to the claimed invention because effective cancer treatment is desirable.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off. Any inquiry of a general nature, matching or filed papers or relating to the status of this application or proceeding should be directed to the Judy Ladringan for Art Unit 1642 whose telephone number is 571-272-0536.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU
PATENT EXAMINER

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Art Unit 1642